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(19)

(54) ESTERS OF PROSTAN-1-OL DERIVATIVES, PROCESS FOR THEIR MANUFACTURE AND PREPARATIONS CONTAINING THEM

(71) We, SCHERING AKTIENGESELLSCHAFT, a Body Corporate organised according to the laws of The Federal Republic of Germany, of Berlin and Bergkamen, The Federal Republic of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

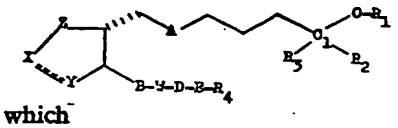
The present invention is concerned with new esters of prostan - 1 - ol derivatives and with their manufacture and use.

It is known that the physiological actions of prostaglandins both in the mammalian organism and *in vitro* are only of short duration, as they are rapidly converted into numerous pharmacologically inactive products of metabolism. It is also known that the natural prostaglandins possess no biological specificity, which is necessary for a medicament.

It has therefore been desired to develop prostaglandin analogues having an action spectrum comparable with that of natural prostaglandins and to bring about structural alterations by means of which the duration and selectivity of the activity is increased.

It has now been found that the prostan - 1 - ol esters of the present invention as defined below, surprisingly possess an outstanding specificity of action and a longer duration of action than do natural prostaglandins. Thus, the compounds of the present invention exhibit, for example, a very good action on the uterus, while the intestinal and vascular musculature is practically unaffected.

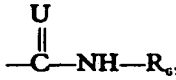
The present invention provides compounds of the general formula I



(I)

in which

R_1 represents an acyl group of an organic carboxylic or sulphonic acid containing 1 to 15 carbon atoms, a group obtainable from an oxygen-containing inorganic acid by the removal of a hydroxyl group, or a group of the formula



in which U represents an oxygen or sulphur atom and R_6 represents an optionally substituted alkyl, cycloalkyl, aryl or heteroaryl group or an acyl group of an organic carboxylic or sulphonic acid,

R_2 and R_3 each represents a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms,

A represents a $—CH_2—CH_2—$, *cis* $—CH=CH—$ or *trans* $—CH=CH—$ group,

B represents a $—CH_2—CH_2—$, *trans* $—CH=CH—$ or $—C\equiv C—$ group or a

group, in which the methylene group is α- or β-positioned,

W represents a free, esterified or etherified hydroxy-methylene group, the hydroxyl group being in the α- or β-position, a free or ketalised carbonyl group or a group of the formula

in which R_7 represents a free, esterified or etherified hydroxyl group in the α- or β-position,

D and E together represent a direct bond, or

D represents a straight chained or branched alkylene group containing 1 to 5 carbon atoms or a —C≡C— group and

E represents an oxygen or sulphur atom or a direct bond,

R_4 represents an unsaturated aliphatic hydrocarbon group, an optionally C_{1-4}-alkyl - substituted cycloalkyl group, an optionally substituted aryl - aliphatic hydrocarbon group, an optionally substituted aryl group, a benzodioxol - 2 - yl group or a monocyclic heterocyclic group and, when D and E together represent a direct bond, or D represents a straight channel or branched alkylene group containing 1 to 5 carbon atoms or a —C≡C— group and E represents an oxygen or sulphur atom or D represents a —C≡C— group and E represents a direct bond, may also represent an alkyl group,

Z represents a carbonyl or a free, esterified or etherified hydroxymethylene group, and

when Z represents a free esterified or etherified hydroxymethylene group, represents a

group, in which the methylene group is α- or β-positioned, or a group of the formula

or

in which R_5 represents an alkyl group or a free, esterified or etherified hydroxyl group, or, when Z represents a carbonyl group, represents a group of the formula

or

in which R'_5 represents an alkyl group or a free or etherified hydroxyl group.

As a

group there is to be understood a substituted carbamoyl or thiocarbamoyl group. As indicated above, the carbamoyl group or thiocarbamoyl group is substituted at the nitrogen atom by an optionally substituted alkyl, cycloalkyl, aryl or heteroaryl group or an acyl group of an organic carboxylic or sulphonic acid.

As alkyl groups represented by R_6 there come into consideration straight or branched alkyl groups containing 1 to 10 carbon atoms for example methyl, ethyl, propyl, isobutyl, butyl, pentyl, heptyl, hexyl and decyl groups.

The alkyl groups represented by R_6 may be substituted one or more times by halogen atoms, alkoxy groups, optionally substituted aryl groups, dialkylamino groups and trialkylammonium groups.

As substituents there may be mentioned, for example, fluorine, chlorine, bromine, phenyl, dimethylamino, diethylamino, methoxy and ethoxy.

As preferred optionally substituted alkyl groups represented by R_6 there should be mentioned methyl, ethyl, propyl, isobutyl, butyl, trichloromethyl and trifluoromethyl groups.

Cycloalkyl groups represented by R_6 are preferably such groups containing 3 to 8 carbon atoms, for example cyclobutyl, cyclopentyl and cyclohexyl groups, but preferably a cyclopropyl group.

As aryl and heteroaryl groups represented by R_6 there come into consideration both substituted and unsubstituted aryl groups and heteroaryl groups, for example phenyl, 1 - naphthyl and 2 - naphthyl groups, each of which may be substituted by 1 to 3 halogen atoms, a phenyl group, 1 to 3 alkyl groups each containing 1 to 4 carbon atoms, of a chloromethyl, fluoromethyl, trifluoromethyl or alkoxy group, and thienyl, furyl and pyridyl groups. Substitution is preferably in the 3- and/or 4-position(s) of the phenyl ring, for example, by fluorine, chlorine, alkoxy or trifluoromethyl.

As acyl groups represented by R_1 and R_6 there come into consideration physiologically tolerable acyl groups, Preferred acids from which the acyl groups are derived are organic carboxylic acids and sulphonic acids containing 1 to 15 carbon atoms, which belong to the

aliphatic, cycloaliphatic, aromatic, aromatic aliphatic or heterocyclic series. These acids may be saturated or unsaturated and/or polybasic and/or substituted in the usual manner. As examples of substituents there may be mentioned alkyl, hydroxyl, alkoxy, oxo or amino groups or halogen atoms.

By way of example there may be mentioned the following carboxylic acids: Formic acid, acetic acid, propionic acid, butyric acid, isobutyric acid, valeric acid, isovaleric acid, caproic acid, oenanthic acid, caprylic acid, perlargonic acid, capric acid, undecanoic acid, lauric acid, tridecanoic acid, myristic acid, pentadecanoic acid, trimethylacetic acid, diethylacetic acid, tert.-butylacetic acid, cyclopentylacetic acid, cyclohexylacetic acid, cyclohexane, carboxylic acid, phenylacetic acid, phenoxyacetic acid, methoxyacetic acid, ethoxyacetic acid, mono- and di- and trichloracetic acids, aminoacetic acid, diethylaminoacetic acid, piperidinoacetic acid, morpholinoacetic acid, lactic acid, succinic acid, adipic acid, benzoic acid, benzoic acids substituted by halogen, trifluoromethyl, hydroxyl, alkoxy or carboxyl groups, nicotinic acid, isonicotinic acid, furan - 2 - carboxylic acid and cyclopentyl - propionic acid. Especially preferred acyl groups are those containing up to 10 carbon atoms.

As sulphonic acids there come into consideration, for example, methane sulphonic acid, ethane sulphonic acid, isopropyl sulphonic acid, β-chlorethane sulphonic acid, butane sulphonic acid, cyclopentane sulphonic acid, cyclohexane sulphonic acid, benzene sulphonic acid, para - toluene sulphonic acid, para - chlorobenzene sulphonic acid, N,N - dimethylamino - sulphonic acid, N,N - diethylamino - sulphonic acid, N,N - bis - (β - chlorethyl) - aminosulphonic acid, N,N - diisobutylamino - sulphonic acid, N,N - dibutylamino - sulphonic acid and pyrrolidino-, piperidino- piperazino-, N - methylpiperazino- and morpholino - sulphonic acids.

There also come into consideration for R_1 acyl groups derived from the usual inorganic acids, for example sulphuric and phosphoric acids.

As alkyl groups represented by R_2 and R_3 there come into consideration straight and branched-chained alkyl groups containing 1 to 4 carbon atoms, for example methyl, ethyl, propyl, isopropyl, butyl, isobutyl and tert. - butyl groups. Preferred are methyl and ethyl groups.

The hydroxyl group represented by R_5 and those in groups represented by W and Z may be functionally converted by etherification or esterification, and the hydroxyl group represented by R'_5 may be functionally converted by etherification; the free or functionally converted hydroxyl groups in groups represented by W and Z may be α- or β-positioned.

As ether-forming and acyl groups for such functional conversion there come into consideration the groups known to the expert. Preferred are ether-forming groups capable of being easily split off, for example tetrahydropyranyl, tetrahydrofuranyl, α - ethoxyethyl, trimethylsolyl, dimethyl - tert. - butyl - silyl and tri - parabenzyl - silyl groups. As acyl groups there come into consideration the same as those given above for R_1, and there may be mentioned especially, for example, acetyl, propionyl, butyryl and benzoyl groups.

When W represents a carbonyl group, the latter may be functionally converted by ketalisation. Especially suitable is the preparation of cyclic ketals containing 1 to 3 carbon atoms in the ring, for example with ethylene glycol, 1,3 - propanediol, 2,2 - dimethyl - 1,3 - propanediol, cyclopentane - 1,2 diol or glycerine.

As aliphatic hydrocarbon groups and optionally substituted aryl - aliphatic hydrocarbon groups represented by R_4 there come into consideration straight and branched-chained, saturated and unsaturated aliphatic hydrocarbon groups, preferably saturated, containing 1 to 10 and especially 1 to 6 carbon atoms, which are optionally substituted by optionally substituted aryl. There may be mentioned, for example, methyl, ethyl, propyl, butyl, isobutyl, tert. - butyl, pentyl, hexyl, heptyl, octyl, butenyl, isobutenyl, propenyl, pentenyl, benzyl and parachlorobenzyl groups.

The cycloalkyl group represented by R_4 may contain in the ring 4 to 10, and preferably 5 to 6, carbon atoms. The rings may be substituted by alkyl groups containing 1 to 4 carbon atoms. There may be mentioned, for example, cyclopentyl, cyclohexyl, methyl - cyclohexyl and adamantyl groups.

As substituted or unsubstituted aryl groups represented by R_4 there come into consideration, for example, phenyl, 1 - naphthyl and 2 - naphthyl groups, each of which may be substituted by 1 to 3 halogen atoms, a phenyl group, 1 to 3 alkyl groups each containing 1 to 4 carbon atoms, or a chloromethyl, fluoro methyl, trifluoromethyl, carbonyl, alkoxy or hydroxyl group.

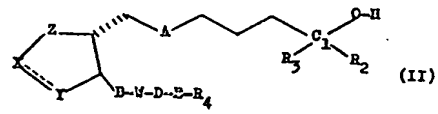
Preferably the substitution is in the 3- and/or 4-position(s) of the phenyl ring, for example by fluorine, chlorine, alkoxy or trifluoromethyl, or in the 4-position by hydroxyl.

As alkyl groups represented by R_5 and R'_5 there come into consideration alkyl groups containing 1 to 2 carbon atoms, preferably methyl groups.

As monocyclic heterocyclic groups represented by R_4 there come into consideration 5- and 6-membered heterocycles, which contain at least one hetero-atom, preferably nitrogen, oxygen or sulphur. By way of example there may be mentioned 2-furyl, 2-thienyl, 2-pyridyl, 3-pyridyl or 4-pyridyl.

The present invention also provides a pro-

cess for the manufacture of the new esters of prostan - 1 - ol derivatives of the general formula I, wherein a compound of the general formula II



(II)

in which
A, Z,

B, W, D, E, R_2, R_3 and R_4 have the meanings given above, is esterified in the 1-position if desired after protecting any other free hydroxyl group present, and then, if desired, in the resulting compound any protected hydroxyl group is liberated and/or any free hydroxyl group is oxidized or esterified and/or any free keto group is ketalised or reduced and/or any double bond is hydrogenated or methylenated and/or by splitting off water in the 10,11 - position from an 11 - hydroxy - 9 - oxo - compound a double bond is introduced, and/or, if desired, any epimers are separated.

The esterification of the alcohols of the general formula II may be carried out in a manner known *per se*. For example, the esterification is carried out by reacting an acid derivative, preferably an acid halide or acid anhydride, in the presence of a base, for example sodium hydride, pyridine, triethylamine, tributylamine or 4 - dimethylaminopyridine, with an alcohol of the general formula II. The reaction may be carried out without a solvent or in an inert solvent, preferably acetone, acetonitrile, dimethylacetamide or DMSO, at temperatures above or below room temperature, for example between —80°C and 100°C, and preferably at room temperature.

Furthermore, for example, an alcohol of the general formula II may be reacted with an isocyanate or thioisocyanate of the general formula III

$$U=C=N-R_6 \qquad \text{(III)}$$

in which

U and R_6 have the meanings given above, optionally with the addition of a tertiary amine, for example triethylamine or pyridine. The reaction may be carried out without a solvent or in an inert solvent, preferably acetone, acetonitrile, dimethylacetamide, methylene chloride, tetrahydrofuran, diethyl ether, benzene, toluene or DMSO, at temperatures above or below room temperature, for example between —80°C and 100°C, and preferably at 0 to 30°C.

When the starting material contains, in addition to the hydroxyl group in the 1-position, additional hydroxyl groups in the prostane group, these hydroxyl groups are also esterified in accordance with the process of the present invention. When final end products are desired, in which additional hydroxyl groups in the prostane group are present in the form of free hydroxyl groups, it is of advantage to start from starting materials in which these are intermediately protected preferably by ether-forming groups capable of being split off easily. When there are used as starting materials compounds which contain in the prostane group esterified or etherified hydroxyl groups, these groups in the end product may be esterified, after liberating the esterified or etherified hydroxyl groups, and different acyl groups may be introduced into the end product.

The liberation of esterified or etherified hydroxyl groups is carried out by known methods. For example, the splitting off of hydroxyl-protecting groups, for example, the tetrahydropyranyl group, is carried out in an aqueous solution of an organic acid, for example acetic acid or propionic acid, or in an aqueous solution of an inorganic acid, for example hydrochloric acid or tetrabutylammonium fluoride. In order to improve solubility it is of advantage to add an inert organic solvent miscible with water. Suitable organic solvents are, for example, alcohols, for example methanol and ethanol, and ethers, for example dimethoxyethane, dioxane and tetrahydrofuran. Tetrahydrofuran is preferably used. The splitting is preferably carried out at tempeatures between 20°C and 80°C.

The ketalisation is carried out in a manner known *per se*, for example, by heating with ethylene glycol in the presence of an acid catalyst with the separation of water. As acid catalysts there are especially suitable para - toluene sulphonic acid and perchloric acid.

The oxidation of hydroxyl groups present is carried out by methods known *per se* with the usual oxidizing agents. For example, oxidation of the 9 - hydroxyl group to form the ketone may be carried out with Jones reagent (J. Chem. Soc. *1953*, 2555). An excess of the oxidizing agent is used in a suitable diluent, for example acetone, at temperatures between 0°C and —50°C, and preferably at —20°C. The reaction generally terminates after 5 to 30 minutes. The oxidation is preferably carried out after intermediate protection of 11- and 15-hydroxyl groups, for example, by silylation (Chem. Comm. (*1972*), 1120). The silylation is carried out, for example, with N,N - diethyl - trimethylsilyl amine in acetone at —70°C to +20°C, and preferably at —40°C to 0°C. As further oxidizing agents there are suitable silver carbonate on "Celite" (Registered Trade Mark) or Collins reagent (Tetrahedron Leters, *1968*, 3363).

The selective oxidation of 9,11-di-hydroxy-compounds, which contain no oxidizable

hydroxyl group in the 15-position, is carried out by methods known to the expert.

For the oxidation of the 11α-hydroxyl group there is preferably used Jones reagent or Collins reagent, and the selective oxidation of the 9α-hydroxyl group is carried out with Fetizon reagent (Tetrahedron *29*, 2867 (1973)), silver carbonate or platinum/oxygen (Adv. in Carbohydrate Chem. *17*, 169 (1962)). The oxidation with Jones reagent is carried out at −40°C to +20°C, and preferably at −30°C to −10°C, or with Collins reagent at −20°C to 30°C, and preferably at 0°C to 20°C, in a solvent inert to the oxidizing agent. As solvents there may be used methylene chloride, chloroform, ethylene chloride and pyridine, but preferably methylene chloride.

As solvents for the oxidation with Fetizon reagent, silver carbonate or platinum with oxygen there may be used benzene, toluene, xylene, ethyl acetate, acetone, tetrahydrofuran, diethyl ether and dioxane and other inert solvents. The reaction temperatures are between 20°C and 110°C in the case of the silver carbonate or Fetizon oxidation, and preferably at the boiling temperature of the solvent. In the oxidation with platinum/oxygen temperatures of preferably 20°C to 50°C are used.

The reduction of the 9-keto group is carried out with the usual reducing agents; for example, it is reduced with sodium borohydride, lithium tri - tert. - butoxy - aluminium hydride, zinc borohydride or aluminium isopropylate in the presence of an alcohol, or potassium tri - sec. - butyl borohydride, and preferably with sodium borohydride at temperatures between −50°C and +50°C, and preferably at 0°C to 20°C. As solvent for this reaction there come into consideration depending on the reducing agent used, methanol, ethanol, isopropanol, diethyl ether, dioxane and tetrahydrofuran. In the reduction with sodium borohydride there is preferably used methanol, ethanol or isopropanol. The α- and β - hydroxyl - epimeric mixture formed may be separated in the usual manner by column or layer chromatography.

If it is desired to reduce C=C double bonds present in the primary product, the hydrogenation is carried out by methods known *per se*.

The hydrogenation of the 5,6-double bond is carried out in a known manner at low temperatures, preferably at −20°C, in an atmosphere of hydrogen in the presence of a noble metal catalyst. There is suitable as catalyst, for example, 10% palladium on charcoal.

If both 5,6- and 13,14 - double bonds are to be hydrogenated, the operation is carried out at a higher temperature, preferably at 20°C.

The dehydration of a 9 - oxo - compound, in which the 11 - hydroxyl group and a hydrogen atom in the 10-position are split off to form a prostaglandin-A derivative, may be carried out under conditions that are generally known to the expert. In general the dehydration is carried out in a solution of an organic acid, for example acetic acid, or an inorganic acid, for example hydrochloric acid, at temperatures between 20°C and 80°C. The reaction terminates after 2 to 17 hours.

The methylenation of the 10,11- and/or 13,14-double bond(s) is carried out in the case of the 9-oxo- or 15-oxo-compounds by methods known *per se*. For example, there may be mentioned reaction with diazo - hydrocarbons, optionally in the presence of metal salts, reaction with dimethyl-sulphoxonium methylide and reaction according to the Simmons-Smith method with zinc and methylene dihalides.

A preferred method consists in reacting the above mentioned compounds with diazohydrocarbons, for example diazomethane, diazoethane and diazopropane, but preferably diazomethane. The reaction is carried out, for example, in the presence of metal salts at temperatures between 20°C and −100°C, and preferably at 0°C, in an inert solvent, for example diethyl ether, tetrahydrofuran, glyme, diglyme or dioxane, but preferably in diethyl ether. As metal salts there may be used copper chloride, copper acetate, palladium-(II) acetate, and palladium-(II) chloride, but preferably palladium-(II) acetate.

The separation of the epimers is carried out by methods known to the expert, for example by a column or layer chromatography or by fractional crystallization.

The preparation of compounds of the general formula II in which R_2 and R_3 each represents a hydrogen atom is carried out by the usual methods, for example, by reducing a corresponding prostanoic acid derivative to form a primary alcohol. Preferable is the reaction of prostanoic acid esters with lithium aluminium hydride.

The preparation of the new compounds of the general formula II, in which R_2 represents an alkyl group containing 1 to 4 carbon atoms and R_3 represents a hydrogen atom, is carried out in the usual manner, for example, by reduction of a prostanoic acid derivative to form the aldehyde. The reduction is preferably carried out upon prostanoic acid esters with diisobutyl-aluminium hydride at −70°C to −40°C in an inert solvent, for example toluene. The subsequent reaction of the aldehyde with a lithium alkyl yields at 0°C in an inert solvent, preferably in diethyl ether and tetrahydrofuran mixtures, the secondary alcohols of the general formula II.

The preparation of the new compounds of the general formula II, in which R_2 and R_3 each represents an alkyl group containing 1 to 4 carbon atoms, is carried out by the usual

methods, for example, by reaction of a prostanoic acid ester with a lithium alkyl at temperatures between −10°C and +10°C, and preferably at 0°C, in an inert solvent, for example diethyl ether and tetrahydrofuran mixtures, with the formation of tertiary alcohols of the general formula.

When free hydroxyl groups are desired in the end product, it is of advantage, before the reduction to the C_1-alcohols, to intermediately protect the optionally present free hydroxyl or free oxo groups, for example, by etherification or ketalisation, respectively.

Preferred compounds of the present invention are, not only the compounds mentioned in the Examples below, but also the following compounds:

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (2 - Carboxy - propionyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 - (2 - Carboxy - propionyloxy) - 16 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

5Z,13E) - (8R,11R,12R,15S,16RS) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - Methoxyacetoxy - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,12S,15S,16RS) - 1 - (2 - Carboxy - propionyloxy) - 16 - methyl - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,12S,15R) - 1 - (2-Carboxy-propionyloxy) - 16,16 - ethylene - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

(13E) - (8R,12S,15S) - 1 - Methoxyacetoxy - 15 - hydroxy - prosta - 10,13, - dien - 9 - one.

(13E) - (8R,12S,15S) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - prosta - 1,13 - dien - 9 - one.

(13E) - (8R,12S,15R) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 10,13 - dien - 9 - one.

(13E) - (8R,12S,15S,16RS) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16 - methyl - prosta - 10,13 - dien - 9 - one.

(5Z) - (8R,12S,15S) - 1 - Methoxyacetoxy - 15 - hydroxy - prosta - 5,10 - dien - 9 - one.

(5Z) - (8R,12S,15S) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - prosta - 5,10 - dien - 9 - one.

(5Z) - (8R,12S,15R) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10 - dien - 9 - one.

(5Z) - 8R,12S,15R,16RS) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16 - methyl - prosta - 5,10 - dien - 9 - one.

(8R,12S,15R) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16,16 - dimethyl - prost - 10 - en - 9 - one.

(8R,12S,15R,16RS) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16 - methyl - prost - 10 - en - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16 - (3 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16 - (3 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16 - (4 - fluorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16 - (4 - fluorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Phenylcarbamoyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,9S,11R,12R,15S) - (1 - (N - Phenylcarbamoyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (N - Phenylcarbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methyl - thiocarbamoyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methyl - thiocarbamoyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (N - Methylthiocarbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 - (N - Methylcarbamoyloxy) - 16 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S,16RS) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S,16RS) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 16 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15R) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R - 1 -(N - Methylcarbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - methylcarbamoyloxy) - 11,15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 17 - phenyl - 18,19,20 - trinor - prosta - 5,3 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,16RS) - 1 - [(N - Methanesulphonyl) - carbamoyloxy] - 16 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S,16RS) - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 16 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - [(N - Methane - sulphonyl) - carbamoyloxy] - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 16,16 - dimethyl - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N Methane - sulphonyl) - carbamoyloxy] - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 16 - (3 - trifluoromethyl-

phenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) -](N - Methane - sulphonyl) - carbamoyloxy] - 16 - (3 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 16 - (3 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 16 - (4 - fluorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - 16 - (4 - fluorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dimethyl - 15 - hydroxy - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Acetyl - carmaboyloxy) - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 - (N - Acetyl - carbamoyloxy) - 16 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S,16RS) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S,16RS) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 16 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E3 - (8R,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 16 - phenoxy 9 - one.

(5Z,13E) - (8R,12S,15R) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N Acetyl - carbamoyloxy) - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5.13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 11.15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9.11.15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Phenyl - carbamoyloxy) - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Phenyl - carbamoyloxy) - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (N - Phenyl - carbamoyloxy) - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S,16RS) - 1 - (N - phenyl - carbamoyloxy) - 16 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S,16RS) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S,16RS) - 1 - (N - phenyl - carbamoyloxy) - 15 - hydroxy - 16 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N -

phenyl - carbamoyloxy) - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15R) - 1 - (N - phenyl - carbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prost - 5.13 - dien - 9 - one.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy) - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy) - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - phenyl - carbamoyloxy) - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien - 9 - one.

5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - methyl - thiocarbamoyloxy) - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - methyl - thiocarbamoyloxy) - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S) - 1 - (N - methyl-thiocarbamoyloxy) - 15 - hydroxy - 15 - methyl - prosta - 5,1,13 - triene - 9 - one.

(5Z,13E) - (8R,11R,12R,15S,16RS) - 1 - (N - methyl - thiocarbamoyloxy) - 11,15 - hydroxy - 16 - methyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15S,16RS) - 1 - (N - methyl - thiocarbamoyloxy) - 15 - hydroxy - 16 - methyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - methyl - thiocarbamoyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,12S,15R) - 1 - (N - methyl - thiocarbamoyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one.

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (N - methyl - thiocarbamoyloxy) - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

(5Z,13E) - (8R,11R,12R,15R) - 1 - (N - methyl - thiocarbamoyloxy) - 16 - phenoxy - 11,15 - dihydroxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

(13E) - 8R,12S,15S,16RS) - 1 - (N - methylcarbamoyloxy) - 15 - hydroxy - 16 - methyl - prosta - 10,13 - dien - 9 - one.

(8R,12S,15S,16RS) - 1 - (N - methyl — carbamoyloxy) - 15 - hydroxy - 16 - methyl - prost - 10 - en - 9 - one.

(13E) - (8R,12S,15S,16RS) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 16 - methyl - prosta - 1,13 - dien - 9 - one.

(8R,12S,15S,16RS) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - 16 - methyl - prost - 10 - en - 9 - one.

(13E) - (8R,12S,15S,16RS) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 16 - methyl - prosta - 10,13 - dien - 9 - one.

(8R,12S,15S,16RS) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 16 - methyl - prost - 10 - en - 9 - one.

(13E) - (8R,12S,15R - 1 - (N - methylcarbamoyloxy) - 16,16 - dimethyl - 15 - hydroxy - prosta - 10,13 - dien - 9 - one.

(8R,12S,15R) - 1 - (N - methylcarbamoyloxy) - 16,16 - dimethyl - 15 - hydroxy - prost - 10 - en - 9 - one.

(13E) - (8R,12S,15R) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 16,16 - dimethyl - 15 - hydroxy - prosta - 10,13 - dien - 9 - one.

(8R,12S,15R) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 16,16 - dimethyl - 15 - hydroxy - prost - 10 - en - 9 - one.

(13E) - (8R,12S,15R) - 1 - (N - Acetyl - carbamoyloxy) - 16,16 - dimethyl - 15 - hydroxy - prosta - 10,13 - dien - 9 - one.

(8R,12S,15R) - 1 - (N - Acetyl - carbamoyloxy) - 16,16 - dimethyl - 15 - hydroxy - prost - 10 - en - 9 - one.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - phenylcarbamoyloxy) - 15 - hydroxy - 11,15 - dimethyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Acetyl - carbamoyloxy) - 15 - hydroxy - 11,15 - dimethyl - prosta - 5,13 - dien - 9 - one.

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 11,15 - dimethyl - prosta - 5,13 - dien - 9 - one.

13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - 11,15 - dimethyl - prost - 13 - en - 9 - one.

The new esters of prostan - 1 - ol derivatives of the general formula I are valuable pharmacological products, as, while having a similar spectrum of action, they have a considerably stronger and above all considerably longer action than do the corresponding natural prostaglandins.

The new prostaglandin analogues of the E-, D- and F- type have a very strong luteolytic action, that is to say, for causing luteolysis considerably smaller dosages are required than in the case of the corresponding natural prostaglandins.

Also for causing abortions, considerably smaller quantities of the new prostaglandin analogues are required than in the case of the natural prostaglandins. The tests were carried out on pregnant rats and guinea-pigs by the usual methods. Thus, pregnant rats were treated subcutaneously from the 4th to 7th day of pregnancy with the compounds of the present invention. On the 9th day the animals were killed and the uteri were examined at the places of nidation. As is shown in the following Table with reference to compounds 1 to 7 as examples, the compounds of the present invention in a 3 to 100 times smaller dose have just as good an abortive action as 1 mg per animal of PG $F_{2\alpha}$. Thus for example, (5Z,13E) - (8R,11R,12R,15R) - 1 - acetoxy - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one, as compared with 1 mg per animal of PG E_2, has just as good an abortive action at a dose 100 times smaller.

TABLE

	Tested compound.	Relative action (PG $F_{2\alpha}$=1) on abortion in the rat.
1	(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol	100
2	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol	10
3	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol	5
4	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - prosta - 5,13 - dien - 9,11,15 - triol	3
5	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol	3
6	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(Methoxy) - acetoxy] - prosta - 5,13 - dien - 9,11,15 - triol	3
7	(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Isobutyryloxy - prosta - 5,13 - dien - 9,11,15 - triol	3

In recording the isotonic uterus contraction of narcotised rats and the isolated rat uterus it is found that the compounds of the present invention are considerably more active and their actions last longer than in the case of the natural prostaglandins.

The new compounds of the present invention are suitable, after a single intrauterine application, for inducing a menstruation or interrupting a pregnancy. It is to be regarded as a therapeutic advance that, in addition to the surprisingly good dissociation of antifertile properties, effects on other organ systems are almost completely prevented. They are also suitable for the synchronisation of the sexual cycle in female mammals, for example apes, rabbits, cattle and pigs.

The good dissociation of action of the compounds of the present invention is shown in the investigation of other unstriated-muscular organs, for example the ileum or guinea-pigs or the isolated trachea of rabbits, where a considerably smaller stimulation is observed than in the case of the natural prostaglandins.

The active compounds of the PG E-series of the present invention exhibit on the isolated trachea of the rabbit *in vitro* a bronchodilatory action and strongly check the secretion of gastric acid and have a regulating action in disturbances of cardiac rhythm. The new compounds of the PG A- and PG E-series also lower the blood pressure and have a diuretic action.

The active compounds of the F-series of the present invention have a less bronchoconstrictive action than does natural prostaglandin $F_{2\alpha}$, which is a great advantage for their therapeutic use. For medicinal use the active substances may be converted into a form suitable for inhalation, or for oral or parenteral application. For inhalation it is of advantage to prepare aerosol or spray solutions.

For oral application there are suitable, for example, tablets, dragees or capsules.

For parenteral administration there are used sterile, aqueous or oily solutions suitable for injection.

The present invention therefore further provides a pharmaceutical preparation which comprises a compound of the general formula I, in admixture or conjunction with a pharmaceutically suitable carrier. The preparations may contain the usual auxiliary and carrier substances.

The active compounds of the present invention serve in combination with the auxiliary substances known and normally used in galenical pharmacy, for example, for the production of preparations for causing an abortion, for controlling menstruation or for inducing a birth. For these purposes there may be used sterile, aqueous solutions, which contain 0.01 to 10 μ grams per ml of active compounds, as an intravenous infusion. The compounds of the general formula I are especially suitable for the preparation of aqueous isotonic solutions. In order to increase solubility there may be added alcohols, for example ethanol, ethylene glycol and propylene glycol.

The following Examples illustrate the invention:

Example 1

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 550 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol, 2.5 ml of pyridine and 1 ml of acetic anhydride was allowed to stand for 14 hours at room temperature. The mixture was evaporated *in vacuo*, and there were obtained 600 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a pale yellow oil.

IR ($CHCl_3$):
1738, 1240/cm.

The 1-acetate so obtained was stirred for 4 hours at 50°C with 15 ml of a mixture of acetic acid/water/tetrahydrofuran (65/35/10), evaporated *in vacuo*, and the residue was purified by column chromatography over silica gel. With diethyl ether/ethyl acetate (8+2) 290 mg of the title compound were obtained in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2930, 2860, 1738, 1240, 972 /cm.
NMR ($CDCl_3$):
δ: 5.3—5.6 (4H,m); 4.06 (2H,t,J=6,5Hz); 3.85—4.28 (3H,m); 8.05 (3H,s); 0.90 (3H,t,J=7Hz).

The starting material for the above compound was prepared as follows:

(a) Prostaglandin $F_{2\alpha}$ - 9,11,15 - tris(tetrahydropyran - 2 - yl) - ether methyl ester.

To a solution of 153 mg of PG $F_{2\alpha}$ methyl ester in 6 ml of methylene chloride were added at 5°C 0.45 ml of dihydropyran and 2 mg of para-toluene sulphonic acid, the mixture was stirred for 30 minutes at 0°C, added to 3 ml of a saturated solution of sodium bicarbonate, diluted with diethyl ether, and the organic phase was agitated twice with water, dried over magnesium sulphate and evaporated *in vacuo*. After filtering the evaporation residue over silica gel, there were obtained with diethyl ether/hexane (1+1) 216 mg of the title compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.75.

(b) (5Z,13E) - (8R,9S,11R,12R,15S) - 9,11,15 - Tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol.

To a suspension of 500 mg of lithium aluminium hydride in 25 ml of diethylether was added dropwise at 10°C a solution of 1 gram of the compound prepared in accordance with Example 1(a) in 25 ml of diethylether, and the whole was stirred for 1.5 hours at room temperature. The excess of lithium aluminium hydride was then destroyed by the dropwise addition of ethyl acetate, 2 ml of water were added, and the mixture was stirred for 45 minutes at room temperature, filtered and evaporated *in vacuo*. After filtering the residue over silica gel, there were obtained with hexane/diethylether (3+2) 880 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2938, 2860, 1600, 975 /cm.
NMR (DMSO-d_6):
δ: 5.2—5.55 (4H,m); 4.45—4.73 (3H,m); 4.3 (1,t,J=5Hz); 0.88 (3H,t,J=7Hz).

Example 2

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Isobutyryloxy - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 300 mg of the compound prepared in accordance with Example 1(b), 2 ml of pyridine and 0.5 ml of isobutyric acid chloride was stirred for 14 hours at room temperature under argon. The mixture was evaporated *in vacuo*, and there was obtained as a crude product (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - isobutyryloxy) - 9,11,15 - tris-(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a yellowish oil, which, without further purification, was stirred with 7 ml of a mixture of acetic acid/water/tetrahydrofuran (65/35/10) for 5 hours at 50°C. After evaporation and chromatography of the residue over silica gel there were obtained with diethylether/ethyl acetate (8+2) 160 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 2938, 2860, 1725, 1160, 973 /cm.
NMR ($CRCl_3$):
δ: 5.23—5.56 (4H,m); 4.05 (2H,t,J=7Hz); 3.8—4.46 (3H,m): 1.16 (6H,d,J=7Hz); 0.90 (3H,t,J=6.5Hz).

Example 3

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - benzoyloxy - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 500 mg of the compound prepared in accordance with Example 1(b), 2 ml of pyridine and 0.5 ml of benzoyl chloride was stirred for 14 hours at room temperature under argon. Then there were added 5 ml of water, the mixture was stirred for 2 hours at room temperature, extracted three times with diethylether, and the organic extract was agitated twice with a saturated solution of sodium bicarbonate, twice with water, dried over magnesium sulphate and evaporated *in vacuo*. There were obtained 545 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - benzoyloxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a colourless oil that was completely unitary according to thin-layer chromatography.

TLC (diethylether/hexane 7+3):
Rf-value 0.78.

The 1 - benzoate so obtained was stirred for 5 hours at 50°C with 15 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10), evaporated *in vacuo*, and the residue was purified by preparative layer chromatography over silica gel plates with diethylether/dioxane (7+3) as entraining agent. There were obtained 245 mg of the title compound in the form of colourless crystals. Melting point 42°C.

TLC (diethylether/dioxane 8+2):
Rf-value 0.27.
IR ($CHCl_3$):
3600, 3420, (wide), 3000, 2938, 2860, 1710, 1600, 1278, 970 /cm.
NMR ($CDCl_3$):
δ: 7.4—7.6 (3H,m); 7.93—8.09 (2H,m); 5.25—5.58 (4H,m); 4.31 (2H,t,J=7Hz); 0.90 (3H,t,J=7Hz).

Example 4

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Butyryloxy - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 300 mg of the compound prepared in accordance with Example 1(b), 2 ml of pyridine and 0.5 ml of butyric anhydride was allowed to stand for 14 hours at room temperature. By evaporation there was obtained in the form of a crude product (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - butyryloxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a pale yellow oil, which, without further purification, was stirred with 7 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 4 hours at 50°C. By evaporation and chromatography of the residue over silica gel there were obtained with diethylether/ethyl acetate (8+2) 172 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2930, 2860, 1737, 972 /cm.

Example 5

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Decanoyloxy - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 200 mg of the compound prepared in accordance with Example 1(b), 1.4 ml of pyridine and 0.4 ml of decanoic acid chloride was allowed to stand for 14 hours at room temperature, 0.2 ml of water was added, and the mixture was allowed to stand for a further 2 hours, diluted with 50 ml of water and extracted three times with 30 ml of diethylether each time, and the organic phase was agitated in succession with a saturated solution of sodium bicarbonate and brine, dried over magnesium sulphate and evaporated to dryness *in vacuo*. The (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - decanoyloxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene so obtained was stirred with 5 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 5 hours at 50°C. After evaporating, chromatography was carried out over silica gel with diethylether/ethyl acetate (9+1), and 150 mg of the title compound were obtained in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 2930, 2860, 1730, 970 /cm.

Example 6

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [Methoxy) - acetoxy] - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 310 mg of the compound prepared in accordance with Example 1(b), 2 ml of pyridine and 0.5 ml of methoxy - acetic acid chloride was stirred for 13 hours at room temperature under argon. The mixture was evapoated *in vacuo*, and there was obtained as a crude product (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(methoxy) - acetoxy] - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a yellowish oil, which, without further purification, was stirred with 7 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 5 hours at 48°C. By evaporation and chromatography of the residue over silica gel there were obtained with diethylether/ethyl acetate (7+3) 158 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3435 (wide), 3000, 2930, 2865, 1740, 975 /cm.

Example 7

(5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1 - Acetoxy - 1 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 700 mg of (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol, 3.7 ml of pyridine and 1.5 ml of acetic anhydride was allowed to stand for 14 hours at room temperature. The mixture was evaporated *in vacuo*, and 770 mg of (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1 - acetoxy - 1 - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene, which was unitary according to thin-layer chromatography, were obtained in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.73.
IR ($CHCl_3$):
3000 2940, 2860, 1727, 1255, 978 /cm.

The 1 - acetate so obtained was stirred for 14 hours at room temperature with 20 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10), evaporated *in vacuo*, and the residue was purified by column chromatography over silica gel. With diethylether/ethyl acetate (8+2) were obtained 385 mg of the title compound in the form of a colourless oil.

TLC (diethylether/dioxane 8+2):
Rf-value 0.29.
IR ($CHCl_3$):
3600, 3430, wide, 3000, 2930, 2860, 1727, 1255, 978 /cm.

The starting material for the above compound was prepared as follows:

(a) (5Z,13E) - (8R,9S,11R,12R,15S) - 9,11,15 - Tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol.

To a solution, cooled to −65°C of 1.68 grams of the compound prepared in accordance with Example 1(a) in 80 ml of toluene were added dropwise 12 ml of a solution of 20% strength of diisobutyl - aluminium hydride in toluene, the mixture was stirred for 15 minutes at =65°C, the excess of reagent was decomposed by the dropwise addition of isopropanol, 6 ml of water were added, the mixture was allowed to warm up to 5°C, stirred for one hour, the precipitate was filtered off, and the filtrate was evaporated to dryness *in vacuo*. There were obtained 1.68 grams of the title compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.68
IR ($CHCl_3$): 3000, 2942, 2860, 2730, 1721, 968 /cm.
NMR (DMSO-d_6):
δ: 9.63 (1H,t,J=2Hz); 5.15—5.55 (4H,m); 4.38—4.73 (3H,m); 0.85 (3H,t,J=6,5Hz).

(b) (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1 - Methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol.

To a solution of 1.68 grams of the aldehyde prepared in accordance with Example 7(a) in 57 ml of diethylether and 57 ml of tetrahydrofuran were added at 0°C under argon 2.84 ml of an approximately 2-molar solution of lithium methyl in diethylether, the mixture was stirred for 20 minutes at 0°C, 50 ml of a saturated solution of ammonium chloride were added, extraction was carried out three times with diethylether, and the organic extract was agitated twice with water, dried over magnesium sulphate and evaporated *in vacuo*. There were obtained 1.61 grams of the title compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.24.
IR: 3600, 3450, 3000, 2940, 2860, 978 /cm.

Example 8

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 1,1 - 1,1 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

A solution of 980 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1,1 - dimethyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol in 30 ml of methylene chloride was mixed with 296 mg of 4 - dimethylaminopyridine and 2.3 ml of

acetic anhydride, and the whole was allowed to stand for 4 days at room temperature. After evaporation *in vacuo*, the residue was filtered with hexane/diethylether (1+1) over silica gel, and there were obtained 985 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 1,1 - dimethyl - 9,11,15 - tris(tetrahydropyran - 2 - xyloxy) - prosta - 5,13 - diene in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.75.
IR ($CHCl_3$):
3000, 2940, 2860, 1723, 1260, 978 /cm.

The 1 - acetate so obtained was stirred for 14 hours at 25°C with 18 ml of a mixture of acetic acid/water/tetrahydrofuran (65/35/10), evaporated *in vacuo*, and the residue was purified by column chromatography over silica gel. With diethylether/ethyl acetate (8+2) there were obtained 380 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3440 (wide), 3000, 2935, 2860, 1724, 1260, 978 /cm.
NMR ($CDCl_3$):
δ: 5.2—5.6 (4H,m); 3.8—4.3 (3H,m); 1.98 (3H,s); 1.42 (6H,s); 0.88 (3H,t,J=7Hz).

The starting material for the above compound was prepared as follows:

(a) (5Z,13E) - (8R,9S,11R,12R,15S) - 1,1 - Dimethyl - 9,11,15 - tris - (tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol.

To a solution of 1.47 grams of the compound prepared in accordance with Example 1(a) in 48 ml of diethylether and 48 ml of tetrahydrofuran were added at 0°C under argon 7 ml of a 2-molar solution of lithium methyl in diethylether. After 20 minutes the mixture was diluted with diethylether, agitated with a saturated solution of sodium chloride, dried with magnesium sulphate, and evaporated *in vacuo*. There were obtained 1.53 grams of the tile compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.31
IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2940, 2860, 978 /cm.

Example 9

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 310 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 15 - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol, 2 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand for 14 hours at room temperature. The mixture was evaporated *in vacuo*, and there was obtained as a crude product (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 15 - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a yellowish oil.

IR ($CHCl_3$):
1738, 1240, 975 /cm.

The 1 - acetate so obtained was stirred for 14 hours at room temperature with 8 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10), the mixture was evaporated *in vacuo*, and the residue was purified by chromatography over silica gel. With diethylether/ethyl acetate (8+2) were obtained 152 mg of the title compound in the form of a colourless oil.

IR:
3595, 3430 (wide), 3000, 2935, 2860, 1738, 1240, 975 /cm.

The starting material for the above compound was prepared as follows:

(a) (15S) - 15 - Methyl - prostaglandin $F_{2\alpha}$ - 9,11,15 - tris(tetrahydropyran - 2 - yl) - ether methyl ester.

To a solution of 160 mg of (15S) - 15 - methyl - PG $F_{2\alpha}$ - methyl ester [Journal of the American Chemical Society, *96* (18), 5865 (1974)] in 6 ml of methylene chloride were added at 5°C 0.5 ml of dihydropyran (freshly distilled) and 2 mg of para-toluene sulphonic acid, the mixture was stirred for 30 minutes at 5°C, added to 4 ml of a saturated solution of sodium bicarbonate, diluted with diethylether, and the organic phase was agitated twice with water, dried over magnesium sulphate and evaporated *in vacuo*. After filtering the evaporation residue over silica gel there were obtained with diethylether/hexane (1+1) 210 mg of the title compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.78.
IR ($CDCl_3$):
1736, 975 /cm.

(b) (5Z,13E) - (8R,9S,11R,12R,15S) - 15 - Methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol.

To a suspension of 100 mg of lithium aluminium hydride in 5 ml of diethylether was added dropwise at 5°C a solution of 0.2 gram of the compound prepared in accordance with Example 9(a) in 5 ml of diethylether, and the whole was stirred for 2 hours at 22°C. The excess of lithium aluminium hydride was then decomposed by the dropwise

addition of ethyl acetate, 0.5 ml of water was added, and the mixture was stirred for 40 minutes at room temperature, filtered and evaporated *in vacuo*. By filtration of the residue over silica gel there were obtained with hexane/diethylether (3+2) 177 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 2998, 2940, 2860, 976 /cm.

Example 10

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

A mixture of 195 mg of (5Z,13E) - (8R,9S,11R,12R,15R) - 16 - phenoxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 1 - ol, 1 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand for 14 hours at room temperature. The mixture was evaporated *in vacuo*, and there were obtained 206 mg of (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - acetoxy - 16 - phenoxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - diene in the form of a colourless oil.

IR ($CHCl_3$):
3000, 2936, 2860, 1728, 1600, 1588, 1495, 1240, 973 /cm.

The 1 - acetate so obtained was stirred for 14 hours at room temperature with 8 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10), the mixture was evaporated *in vacuo*, and the residue was purified by layer chromatography over silica gel plates. With diethylether/dioxane (8+2) there were obtained 72 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3595, 3440, 3000, 2940, 2860, 1728, 1600, 1588, 1495, 1240, 975 /cm.

The starting material for the above compound was prepared as follows:

(a) (5Z,13E) - (8R,9S,11R,12R,15R) - 16 - Phenoxy - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dienoic acid methyl ester.

To a solution of 140 mg of (5Z,13E) - (8R,9S,11R,12R,15R) - 16 - phenoxy - 9,11,15 - trihydroxy - 17,18,19,20 - tetranor - prosta - dienoic acid methyl ester (see German Offenlegungsschriften 2,223,365 and 2,322,673) in 4.5 ml of methylene chloride were added at 5°C 0.14 ml of dihydropyran and 1.5 mg of para - toluene sulphonic acid, the mixture was stirred for 30 minutes at 5°C, added to 4 ml of a saturated solution of sodium bicarbonate, diluted with diethylether, and the organic phase was agitated twice with water, dried over magnesium sulphate and evaporated *in vacuo*. After filtration of the residue over silica gel there were obtained with diethylether/hexane (1+1) 205 mg of the title compound in the form of a colourless oil.

TLC (diethylether/hexane 7+3):
Rf-value 0.71.

(b) (5Z,13E) - (8R,9S,11R,12R,15R) - 16 - Phenoxy - 9,11 - tris(tetrahydropyran - 2 - yloxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 1 - ol.

To a suspension of 122 mg of lithium aluminium hydride in 7 ml of diethylether was added dropwise at 5°C a solution of 238 mg of the compound prepared in accordance with Example 10(a) in 7 ml of diethylether, and the whole was stirred for 2 hours at room temperature. The excess of reagent was then decomposed by the dropwise addition of ethyl acetate, 0.8 ml of water was added, and the mixture was stirred for 40 minutes at room temperature, filtered and evaporated *in vacuo*. After filtration of the residue over silica gel there were obtained with diethylether/hexane (3+2) 196 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430, 3000, 2940, 2860, 1600, 1588, 1495, 975 /cm.

Example 11

By proceeding as in Example 10, but with the use of (5Z,13E) - (8R,9S,1R,12R,15R) - 16 - (3 - trifluoromethylphenoxy) - 9,11,15 - trihydroxy - 17,18,19,20 - tetranor - prosta - 5,13 - dienoic acid methyl ester (see German Offenlegungsschriften 2,223,365 and 2,322,673), there was obtained (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - acetoxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430, 3000, 2940, 2860, 1730, 1600, 1592, 1490, 1240, 975 /cm.

Example 12

By proceeding in accordance with Example 10, but with the use of (5Z,13E) - (8R,9S,11R,12R,15R) - 16 - (4 - chlorophenoxy) - 9,11,15 - trihydroxy - 17,18,19,20 - tetranor - prosta - 5,13 - dienoic acid methyl ester (see German Offenlegungsschriften 2,223,365 and 2,322,673), there was obtained (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - acetoxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 -

tetranor - prosta - 5,13 - dien - 9,11,15 - triol in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2950, 2860, 1730, 1600, 1583, 1492, 1245, 975, 872, 828 /cm.

Example 13

By proceeding in accordance with Example 10, but with the use of (5Z,13E) - (8R,9S,11R,12R,15S) - 17 - phenyl - 9,11,15 - trihydroxy - 18,19,20 - trinor - prosta - 5,13 - dienoic acid methyl ester (German Offenlegungsschrift 2,234,709), there was obtained (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3400 (wide), 3000, 2960, 1860, 1732, 1600, 1250, 975 /cm.

Example 14

By proceeding in accordance with Example 10, but with the use of (5Z,13E) - (8R,9S,11R,12R,15S) - 9,15 - dihydroxy - 11 - methyl - prosta - 5,13 - dienoic acid methyl ester (see Chemistry and Industry *1973*, 635), there was obtained (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - acetoxy - 11 - methyl - prosta - 5,13 - dien - 9,15 - diol in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2950, 2860, 1725, 1260, 978 /cm.

Example 15

By proceeding in accordance with Example 10, but with the use of (5Z,13E) - (8R,9S,11R,12R,15R) - 16,16 - dimethyl - 9,11,15 - trihydroxy - prosta - 5,13 - dienoic acid methyl ester (see German Offenlegungsschrift 2,221,301), there was obtained (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - acetoxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2940, 2860, 1730, 1255, 978 /cm.

Example 16

(5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

To a solution of 93 mg of the 1-acetate prepared in accordance with Example 1 in 4 ml of obsolute acetone were added at −45°C 1.2 ml of N,N - diethyl - trimethylsilylamine, and the whole was stirred for 6.5 hours at −40°C. The mixture was then diluted with 30 ml of diethylether, which had previously been cooled to −70°C, the mixture was agitated once with 5 ml of an ice-cooled solution of sodium bicarbonate and twice with 5 ml of a saturated solution of sodium chloride each time, dried with sodium sulphate and evaporated *in vacuo*. The 11,15 - bis(trimethylsilyl ether) obtained in this manner was dissolved in 16 ml of absolute methylene chloride, and a solution of 665 mg of Collins reagent (for preparation see Org. Syntheses Vol. *52*, 5) was added at +5°C, and the mixture was stirred for 10 minutes, diluted with 50 ml of diethylether, filtered and evaporated *in vacuo*. In order to split off the silyl ether protecting groups the residue was stirred with a mixture of 9 ml of methanol, 0.9 ml of water and 0.45 ml of glacial acetic acid for 45 minutes at room temperature. The mixture was then diluted with 60 ml of diethylether, agitated with 10 ml of sodium bicarbonate solution, twice with 10 ml of a saturated solution of sodium chloride each time, dried over magnesium sulphate and evaporated in vacuo. After purification by preparative layer chromatography (diethylether/dioxane 9+1 as entraining agent) over silica gel plates there were obtained 55 mg of the title compound in the form of a colourless oil.

TLC (diethylether/dioxane 9+1):
Rf-value 0.35.

IR ($CHCl_3$):
3600, 3400 (wide), 2998, 2960, 2930, 2860, 1738, 1730, 1602, 973 /cm.
NMR ($CDCl_3$):
δ: 5.50—5.68 (2H,m); 5.22—5.44 (2H,m); 4.03 (2H,t,J=7Hz); 3.93—4.18 (1H,m); 3,62—3.82 (1H,m); 2.05 (3H,s); 0.90 (3H,t,J=7Hz).

Example 17

(5Z,13E) - (8R,11R,12R,15S) - 1 - Isobutyryloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - isobutyrate prepared in accordance with Example 2 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 2998, 2938, 2860, 1740, 1725, 1160, 975 /cm.

Example 18

(5Z,13E) - (8R,11R,12R,15S) - 1 - Benzoyloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - benzoate prepared in accordance with Example 3 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3425 (wide), 3000, 2940, 2860, 1740, 1712, 1600, 1278, 973 /cm.

Example 19

(5Z,13E) - (8R,11R,12R,15S) - 1 - Decanoyloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - decanoate prepared in accordance with Example 5 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2930, 2860, 1738, 1730, 970 /cm.

Example 20

(5Z,13E) - (8R,11R,12R,15S) - 1 - Butyryloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - butyrate prepared in accordance with Example 4 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 300, 2930, 2960, 1738 (wide), 974 /cm.

Example 21

(5Z,13E) - (8R,11R,12R,15S) - 1 - [(Methoxy) - acetoxy] - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - methoxyacetate prepared in accordance with Example 6 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3440 (wide), 3000, 2933, 2865, 1740 (wide), 975 /cm.

Example 22

(5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 1 - methyl - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - methyl - 1 - acetate prepared in accordance with Example 7 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2930, 2860, 1738, 1727, 1255, 978 /cm.

Example 23

(5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 1,1 - dimethyl - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1,1 - dimethyl - 1 - acetate prepared in accordance with Example 8 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3595, 3410 (wide), 2960, 2930, 2860, 1738, 1720, 1600, 1265, 970 /cm.

Example 24

(5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 9 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 2930, 2860, 1738 (wide), 1245, 975 /cm.

Example 25

(5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 10 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3440 (wide), 2940, 2860, 1738, 1728, 1600, 1588, 1495, 1240, 975 /cm.

Example 26

(5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 11, the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2940, 2860, 1738, 1730, 1600, 1595, 1490, 1240, 975 /cm.

Example 27

(5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 12 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2945, 2860, 1738, 1730, 1600, 1583, 1492, 1245 976, 875, 830 /cm.

Example 28

(5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 13 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3400 (wide), 3000, 2960, 2860, 1738, 1731, 1600, 1250, 975 /cm.

Example 29

(5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 15 - hydroxy - 11 - methyl - prosta - 5.13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 14 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3430 (wide), 3000, 2950, 2860, 1738, 1725, 1260, 978 /cm.

Example 30

(5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 16 there was obtained from the 1 - acetate prepared in accordance with Example 15 the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3420, (wide), 2940, 2860, 1738, 1730, 1255, 975 /cm.

Example 31

(5Z,13E) - (8R,12S,15S) - 1 - Acetoxy - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

A mixture of 100 mg of the 1 - acetate prepared in accordance with Example 16 with 8 ml of an aqueous acetic acid of 90% strength was stirred for 14 hours at 60°C. The mixture was then evaporated *in vacuo*, and the residue was purified by preparative layer chromatography (diethylether) over silica gel plates. There were obtained 68 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3460 (wide), 3000, 2960, 2935, 2860, 1735, 1702, 1240, 970 /cm.
NMR (DCl_3):
δ: 7.45 (1H,dd,J=6+2,5Hz); 6.13 (1H,dd,J=6+2Hz); 4.08 (2H,t,J=6.5 Hz); 8.05 (3H,s); 0.90 (3H,t,J=6.5Hz).

Example 32

(5Z,13E) - (8R,12S,15S) - 1 - Acetoxy - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.

A mixture of 95 mg of the 1 - acetate prepared in accordance with Example 24 with 8 ml of aqueous acetic acid of 90% strength was stirred for 16 hours at 60°C. The mixture was then evaporated *in vacuo*, and the residue was purified by preparative layer chromatography (diethylether) over silica gel plates. There were obtained 60 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3450 (wide), 3000, 2960, 2935, 2860, 1735, 1702, 1240, 974 /cm.

Example 33

(5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1,9,11,15 - Tetracetoxy - 1 - methyl - prosta - 5,13 - diene.

A mixture of 530 mg of (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1 - methyl - 9,11,15 - tris(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 1 - ol (for preparation see Example 7(b)) and 20 ml of a mixture of acetic acid/water/tetrahydrofuran (65/35/10) were stirred for 14 hours at room temperature under argon. The mixture was then evaporated *in vacuo*, and the residue was purified by chromatography over silica gel. With diethylether/isopropanol (9+1) were obtained 210 mg of (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1,9,11,15 - tetrahydroxy - 1 - methyl - prosta - 5,13 - diene in the form of a colourless oil.

TLC (diethylether/dioxane 7+3):
0.21.

The tetrol prepared in this manner was allowed to stand at room temperature for 14 hours with a mixture of 0.2 ml of acetic anhydride and 0.8 ml of pyridine. After evaporation, the tetra - acetate was purified by filtration over silica gel. With diethylether/hexane (8+2) were obtained 280 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3000, 2960, 2935, 2860, 1735, 1240, 975 /cm.

Example 34

(5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15- triol.

200 mg of (5Z,13E) - (8R,9S,11R,12R,15R)- 1 - (2 - carboxy - propionyl) - 16,16 - dimethyl - 9 - tribenzylsilyloxy - 11,15 - bis'tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien in 10 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) were stirred for 14 hours at room temperatue, the mixture was evaporated *in vacuo*, and the residue was purified by column chromatography over silica gel. With methyl chloride/isopropanol (7+3) were obtained 72 mg of

the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 2940, 1728, 976 /cm.

The starting material for the above reaction was prepared as follows:

3.6 Grams of 16,16 - dimethyl - prostaglandin $F_{2\alpha}$ methyl ester - 11,15 - bis(tetrahydropyranyl) ether (prepared in accordance with German Offenlegungsschrift 2,221,301 from the acid with diazomethane) dissolved in 54 ml of pyridine were mixed with 2.82 grams of tribenzylsilyl chloride, and the whole was stirred for 3 hours at 48°C under argon. The solvent was distilled off *in vacuo* at 15 Torr, and the residue was chromatographed over silica gel. With diethylether/pentane mixtures 4.2 grams of the corresponding 9 - tribenzylsilyl ether were eluted in the form of a colourless oil.

To 4.2 grams of the silyl ether in 180 ml of absolute diethylether were added at 20°C in portions 1.20 grams of lithium aluminium hydride, the mixture was stirred for 3 hours at 20°C, the excess of reagent was decomposed by the dropwise addition of ethyl acetate, 2.8 ml of water were added, and the mixture was stirred for one hour, filtered and evaporated *in vacuo*. 830 mg of the 1 - alcohol so obtained were dissolved in 1.5 ml of pyridine, 120 mg of succinic anhydride were added, and the whole was stirred for 16 hours at 20°C. 10 ml of water were then added, the mixture was stirred for 15 minutes, extracted with diethylether, and the extract was agitated with brine, dried over magnesium sulphate and evaporated to dryness *in vacuo*. By filtration over silica gel with methylene chloride were obtained 530 mg of (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyl) - 16,16 - dimethyl - 9 - tribenzylsilyloxy - 11,15 - bis(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene in the form of a colourless oil.

IR ($CHCl_3$):
2940, 1728, 1600, 1495, 1165, 1020, 978 /cm.

Example 35

(5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.

265 mg of (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16,16 - dimethyl - 11,15 - bis(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - one were stirred with 7 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 5 hours at 40°C, and then the mixture was evaporated to dryness *in vacuo*. The oily residue was purified by chromatography over silica gel. With methylene chloride/isopropanol (8+2) there were obtained 90 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 2940, 1738 (shoulder), 1728, 978 /cm.

The starting material was prepared as follows:

750 mg of (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - carboxy - propionyloxy) - 16,16 - dimethyl - 9 - tribenzylsilyloxy - 11,15 - bis-(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - diene and 223 mg of tetrabutyl - ammonium fluoride were stirred in 60 ml of tetrahydrofuran for 2 hours at 0°C, the mixture was diluted with water, acidified with citric acid of 10% strength to a pH-value of 5, extracted with diethylether, and the organic extract was agitated with brine, dried over magnesium sulphate and evaporated to dryness *in vacuo*. By filtration over silica gel with diethylether there were obtained 430 mg of the 9 - hydroxy - compound in the form of a colourless oil.

IR ($CHCl_3$):
3500 (wide), 2940, 1728, 1468, 1452, 1440, 1125, 1020, 978 /cm.

300 mg of the 9 - hydroxy - compound obtained above were dissolved in 7 ml of acetone and 0.25 ml of Jones reagent was added dropwise at −20°C. After 25 minutes the excess of reagent was decomposed by the addition of isopropanol, and the mixture was diluted with diethylether and agitated until neutral with brine. By drying over magnesium sulphate and evaporation there were obtained 270 mg of the 9 - keto - compound in the form of a colourless oil.

IR ($CHCl_3$):
3600 (wide), 2940, 1738 (shoulder), 1730, 978 /cm.

Example 36

(5Z,13E) - (8R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one.

A mixture of 200 mg of (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - carboxy - propionyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one and 15 ml of acetic acid of 90% strength was stirred for 16 hours at 60°C. The mixture was then evaporated *in vacuo*, and the residue was purified by preparative layer chromatography (silica gel, methylene chloride/isopropanol 9+1). There were obtained 105 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3500 (wide), 2940, 1730, 1602, 976 /cm.

Example 37

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.

To a solution of 300 mg of the 1 - alcohol obtained in accordance with Example 37(b) in 5 ml of absolute tetrahydrofuran were added in succession 1.2 ml of methyl isocyanate and 3 drops of triethylamine, the mixture was allowed to stand overnight at room temperature, evaporated to dryness *in vacuo*, and the residue was purified by filtration over silica gel with diethylether/pentane (1:1). There were obtained 305 mg of the corresponding urethane in the form of a colourless oil.

IR ($CHCl_3$):
3470, 2943, 1700, 1650, 1020, 975 /cm.

250 mg of (5Z,13E) - (8R,9S,11R,12R,15S)-1 - (N - methyl - carbamoyloxy) - 11,15 - bis(tetrahydropyran - 2 - yloxy) - 9 - tribenzylsilyloxy - prosta - 5,13 - diene were stirred in 15 ml of a mixture of glacial acetic acid/water/tetrahydrofuran (65/35/10) for 5 hours at 50°C, evaporated *in vacuo* and the residue was purified by chromatography over silica gel with diethylether/dioxane (7+3). There were obtained 105 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3605, 3470, 2935, 1700, 1650, 1512, 1080, 972, 947 /cm.
NMR ($CDCl_3$):
δ 5.3—5.6 m, 4H olefinic protons.
3.8—4.3 m, 5H carbinolic proton and

$$—CH_2—CH_2—O.$$

2.85 d, 6Hz

$$—NH—CH_3.$$

2.78 d, 7Hz
0.88 t 7Hz 3H, $—CH_2—CH_3$.

The starting material for the above reaction was prepared as follows:

(a) 1.80 Grams of prostaglandin $F_{2\alpha}$ methyl ester - 11,15 - bis - (tetrahydropyranyl) ether (obtained from the corresponding acid, see J. Amer. Chem. Soc. *91*, 5675 (1969), with diazomethane) dissolved in 25 ml of pyridine were mixed with 1.40 grams of tribenylsilyl chloride, and the whole was stirred for 5 hours at 50°C under argon. After distilling off the solvent *in vacuo*, the oily residue was chromatographed over silica gel with diethylether/pentane mixtures. There were obtained 2.05 grams of the corresponding 9 - tribenzylsilyl ether in the form of a colourless oil.

(b) To 2.05 grams of silyl ether in 80 ml of absolute diethylether was added in portions at room temperature 0.5 gram of lithium aluminium hydride, and the mixture was stirred for 2 hours at 20°C, the excess of reagent was decomposed with ethyl acetate, 1.2 ml of water were added, and the mixture was stirred for one hour at 20°C, filtered and evaporated *in vacuo*. There were obtained 1.95 grams of (5Z,13E) - (8R,9S,11R,12R,15S) - 11,15 - bis(tetrahydropyran - 2 - yloxy) - 9 - tribenzylsiloxy - prosta - 5,13 - dien - 1 - ol, which was completely unitary according to thin-layer chromatography.

The IR-spectrum (in chloroform) no longer exhibited carbonyl vibration.

Example 38

(5Z,13E) - (8R,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

300 mg of (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - methylcarbamoyloxy) - 11,15 - bis-(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - one were stirred with 9 ml of a mixture of the glacial acetic acid/water/tetrahydrofuran (65/35/10) for 6 hours at 40°C, and the mixture was then evaporated to dryness *in vacuo*. After purifying the residue by chromatography over silica gel (diethylether/ethyl acetate 7+3) 145 mg of the title compound were obtained in the form of a colourless oil.

IR ($CHCl_3$):
3605, 3470, 2940, 1735, 1700, 1650, 1512, 1085, 972, 948 /cm.

The starting material for the above reaction was prepared as follows:

(a) A solution of 370 mg of the 9,11,15 - protected urethane prepared in accordance with Example 37 and 110 mg of tetrabutyl - ammonium fluoride in 30 ml of tetrahydrofuran was stirred for 2 hours at 0°C, the mixture was diluted with water, extracted with diethylether, and the organic extract was agitated with brine, dried over magnesium sulphate and evaporated to dryness *in* vacuo. By filtration over silica gel with diethylether there were obtained 205 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - methylcarbamoyloxy) - 11,15 - bis (tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - ol in the form of a colourless oil.

(b) To a solution of 290 mg of the 9 - hydroxy - compound obtained above in 8 ml of acetone was added dropwise at −20°C 0.25 ml of Jones reagent, and the whole was stirred for 25 minutes at −20°C, the excess of reagent was decomposed by the addition of isopro-

panol, and the mixture was diluted with diethylether and agitated until neutral with brine. After drying over magnesium sulphate and evaporating, there were obtained 265 mg of (5Z,13E) - (8R,11R,12R,15S) - 1 - (N - methylcarbamoyloxy) - 11,15 - bis(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - one in the form of a colourless oil.

IR, $CHCl_3$):
3470, 2945, 1735, 1700, 1650, 1080, 972, 948 /cm.

Example 39

(5Z,13E) - (8R,12S,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

250 mg of the PGE-derivative prepared in accordance with Example 38 in 16 ml of acetic acid of 90% strengh were stirred for 16 hours at 60°C, evaporated *in vacuo*, and the residue was purified by preparative layer chromatography (silica gel, diethylether). 165 mg of the title compound were obtained in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3500 (wide), 2940, 1700, 1602, 978 /cm.

Example 40

(5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - prosta - 5,13 - dien - 9,11,15 - triol.

To a solution of 405 mg of the 1-alcohol obtained in accordance with Example 37(b) in 10 ml of absolute toluene were added at 0°C 145 mg of methane - sulphonyl isocyanate, and the whole was stirred for 1 hour at 20—25°C, water was added, the mixture was extracted by agitation with diethylether, and the extract was washed with brine, dried over magnesium sulphate and evaporated *in vacuo*. After filtering the residue over silica gel with methylene chloride there were obtained 390 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 11,15 - bis(tetrahydropyran - 2 - yloxy) - 9 - tribenzyloxy - prosta - 5,13 - diene in the form of a colourless oil.

From 300 mg there were obtained in the manner analogous to that in Example 37 120 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3380, 1720, 1400, 1346, 1020, 975 /cm.

Example 41

(5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

In a manner analogous to that in Example 38 there were obtained from 250 mg of (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 11,15 - bistetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - one 112 mg of the title compound in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3400, 2940, 1735 (shoulder), 1720, 1400, 1345, 1020, 976 /cm.

The starting material for the above reaction was obtained as follows:

(a) In a manner analogous to that in Example 38(a) there were obtained from 400 mg of the 9 - tribenylsilyloxy-compound prepared in accordance with Example 40 and 120 mg of tetrabutylammonium fluoride 210 mg of (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 11,15 - bis(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - ol in the form of a colourless oil.

(b) In a manner analogous so that in Example 38(b) there were obtained from 210 mg of the compound prepared as above and 0.2 ml of Jones reagent 170 mg of (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - methane - sulphonyl) - carbamoyloxy] - 11,15 - bis(tetrahydropyran - 2 - yloxy) - prosta - 5,13 - dien - 9 - one in the form of a colourless oil.

Example 42

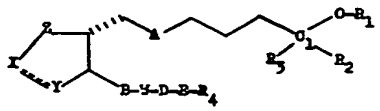
(5Z,13E) - (8R,12S,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

200 mg of PGE-derivative prepared in accordance with Example 41 in 12 ml of acetic acid of 90% strength were stirred for 16 hours at 60°C, the mixture was evaporated *in vacuo*, and the residue was purified by preparative layer chromatography (silica gel, methylene chloride/isopropanol 9+1). 105 mg of the title compound were obtained in the form of a colourless oil.

IR ($CHCl_3$):
3600, 3500, 2944, 1710, 1603, 978 /cm.

WHAT WE CLAIM IS:—

1. A compound of the general formula I

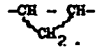


(I)

in which

R_1 represents an acyl group of an organic carboxylic or sulphonic acid containing 1 to 15 carbon atoms or a group obtain-

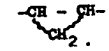
able from an oxygen-containing inorganic acid by the removal of a hydroxyl group,
R_2 and R_3 each represents a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms,
A represents a $-CH_2-CH_2-$, *cis* $-CH=CH-$ or *trans* $-CH=CH-$ group,
B represents a $-CH_2-CH_2-$, *trans* $-CH=CH-$ or $-C\equiv C-$ group or a



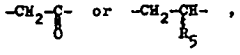
group, in which the methylene group is α- or β-positioned,
W represents a free, esterified or etherified hydroxy - methylene group, the hydroxyl group being in the α- or β-position, a free or ketalised carbonyl group or a group of the formula

in which
R_7 represents a free, esterified or etherified hydroxyl group in the α- or β-position.
D and E together represent a direct bond, or
D represents a straight chained or branched alkylene group containing 1 to 5 carbon atoms or a $-C\equiv C-$ group and
E represents an oxygen or sulphur atom or a direct bond,
R_4 represents an unsaturated aliphatic hydrocarbon group, an optionally C_{1-4}-alkyl-substituted cycloalkyl group, an optionally substituted aryl-aliphatic hydrocarbon group, an optionally substituted aryl group, a benzodioxol - 2 - yl group or a monocyclic heterocyclic group and, when D and E together represent a direct bond, or D represents a straight chained or branched alkylene group containing 1 to 5 carbon atoms or a $-C\equiv C-$ group and E represents an oxygen or sulphur atom or D represents a $-C\equiv C-$ group and E represents a direct bond, may also represent an alkyl group,
Z represents a carbonyl or a free, esterified or etherified hydroxymethylene group, and

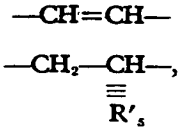
when Z represents a free, esterified or etherified hydroxymethylene group, represents a



group, in which the methylene group is α- or β-positioned, or a group of the formula

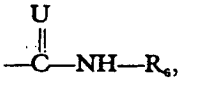


in which
R_5 represents an alkyl group or a free esterified or etherified hydroxyl group, or, when Z represents a carbonyl group, represents a group of the formula



in which
R'_5 represents an alkyl group or a free or etherified hydroxyl group.

2. A compound of the general formula I given in claim 1, in which R_1 represents a group of the formula



in which
U represents an oxygen or sulphur atom and
R_6 represents an optionally substituted alkyl, cycloalkyl, aryl or heteroaryl group or an acyl group of an organic carboxylic or sulphonic acid, and
R_3, R_2, A, B, W. D. E, R_4, Z and

have the meanings given in claim 1.

3. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - prosta - 5,13 - dien - 9,11,15 triol.

4. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Isobutyryloxy - prosta - 5,13 - dien - 9,11,15 - triol.

5. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Benzoyloxy - prosta - 5,13 - dien - 9,11,15 - triol.

6. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Butyryloxy - prosta - 5,13 - dien - 9,11,15 - triol.

7. (5Z,13E - (8R,9S,11R,12R,15S) - 1 - (Decanoyloxy - prosta - 5,13 - dien - 9,11,15 - triol.

8. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(Methoxy) - acetoxy] - prosta - 5,13 - dien - 9,11,15 - triol.

9. (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1 - Acetoxy - 1 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

10. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 1,1 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

11. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 -

Acetoxy - 15 - methyl - prosta - 5,13 - dien - 9,11,15 - triol.

12. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

13. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

14. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9,11,15 - triol.

15. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9,11,15 - triol.

16. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - Acetoxy - 11 - methyl - prosta - 5,13 - dien - 9,15 - diol.

17. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - Acetoxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

18. (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

19. (5Z,13E) - (8R,11R,12R,15S) - 1 - Isobutyryloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

20. (5Z,13E) - (8R,11R,12R,15S) - 1 - Benzoyloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

21. (5Z,13E) - (8R,11R,12R,15S) - 1 - Decanoyloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

22. (5Z,13E) - (8R,11R,12R,15S) - 1 - Butyryloxy - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

23. (5Z,13E) - (8R,11R,12R,15S) - 1 - [(Methoxy) - acetoxy] - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

24. (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 1 - methyl - prosta - 5,13 - dien - 9 - one.

25. (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 1,1 - dimethyl - prosta - 5,13 - dien - 9 - one.

26. (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 15 - methyl - prosta - 5,13 - dien - 9 - one.

27. (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - phenoxy - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

28. (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - (3 - trifluoromethylphenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

29. (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16 - (4 - chlorophenoxy) - 17,18,19,20 - tetranor - prosta - 5,13 - dien - 9 - one.

30. (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 11,15 - dihydroxy - 17 - phenyl - 18,19,20 - trinor - prosta - 5,13 - dien - 9 - one.

31. (5Z,13E) - (8R,11R,12R,15S) - 1 - Acetoxy - 15 - hydroxy - 11 - methyl - prosta - 5,13 - dien - 9 - one.

32. (5Z,13E) - (8R,11R,12R,15R) - 1 - Acetoxy - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.

33. (5Z,13E) - (8R,12S,15S) - 1 - Acetoxy - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

34. (5Z,13E) - (8R,12S,15S) - 1 - Acetoxy - 15 - hydroxy - 15 - methyl - prosta - 5,10,13 - trien - 9 - one.

35. (5Z,13E) - (1RS,8R,9S,11R,12R,15S) - 1,9,11,15 - Tetracetoxy - 1 - methyl - prosta - 5,13 - diene.

36. (5Z,13E) - (8R,9S,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 16,16 - dimethyl - prosta - 5,13 - dien - 9,11,15 - triol.

37. (5Z,13E) - (8R,11R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 11,15 - dihydroxy - 16,16 - dimethyl - prosta - 5,13 - dien - 9 - one.

38. (5Z,13E) - (8R,12R,15R) - 1 - (2 - Carboxy - propionyloxy) - 15 - hydroxy - 16,16 - dimethyl - prosta - 5,10,13 - trien - 9 - one.

39. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - (N - Methylcarbamoyloxy) - prosta - 5,13 - dien - 9,11,15 - triol.

40. (5Z,13E) - (8R,11R,12R,15S - 1 - (N - Methylcarbamoyloxy) - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

41. (5Z,13E) - (8R,12S,15S) - 1 - (N - Methylcarbamoyloxy) - 15 - hydroxy - prosta - 5,10,13 - 9 - one.

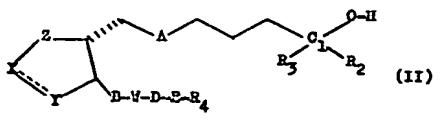
42. (5Z,13E) - (8R,9S,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - prosta - 5,13 - dien - 9,11,15 - triol.

43. (5Z,13E) - (8R,11R,12R,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 11,15 - dihydroxy - prosta - 5,13 - dien - 9 - one.

44. (5Z,13E) - (8R,12S,15S) - 1 - [(N - Methane - sulphonyl) - carbamoyloxy] - 15 - hydroxy - prosta - 5,10,13 - trien - 9 - one.

45. Any one of the compounds as claimed in claim 1 and described in Examples 1 to 10, 34, 35, 37, 38, 40 and 41 herein, excluding the compounds claimed in claims 3 to 12, 36, 37, 39, 40, 42 and 43.

46. A process for the manufacture of a compound as claimed in claim 1, wherein a compound of the general formula II



(II)

in which

A, Z,

B, W, D, E, R_2, R_3 and R_4 have the meanings given in claim 1, is esterified

in the 1-position, if desired after protecting any other free hydroxyl group present, and then, if desired, in the resulting compound any protected hydroxyl group is liberated and/or any free hydroxyl group is oxidized or esterified and/or any free keto group is ketalised or reduced and/or any double bond is hydrogenated or methylated and/or by splitting off water in the 10,11-position from an 11 - hydroxy - 9 - oxo - compound a double bond is introduced, and/or, if desired, any epimers are separated.

47. A process for the manufacture of a compound as claimed in claim 2, wherein a compound of the general formula II given in claim 46,
in which
A, Z,

B, W, D, E. R_2, R_3 and R_4 have the meanings given in claim 1, is esterified in the 1-position, if desired after protecting any other free hydroxyl group present, and then, if desired, in the resulting compound any protected hydroxyl group is liberated and/or any free hydroxyl group is oxidized or esterified and/or any free-keto group is ketalised or reduced and/or any double bond is hydrogenated or methylated and/or by splitting off water in the 10,11-position from an 11 - hydroxy - 9 - oxo - compound a double bond is introduced, and/or, if desired, any epimers are separated.

48. A process as claimed in claim 46 or 47, conducted substantially as described herein.

49. A process for the manufacture of a compound as claimed in claim 1, conducted substantially as described in any one of Examples 1 to 33 herein.

50. A process for the manufacture of a compound as claimed in claim 1, conducted substantially as described in any one of Examples 34 to 36 herein.

51. A process for the manufacture of a compound as claimed in claim 2, conducted substantially as described in any one of Examples 37 to 42 herein.

52. A pharmaceutical preparation which comprises a compound as claimed in claim 1, in admixture or conjunction with a pharmaceutically suitable carrier.

53. A pharmaceutical preparation which comprises a compound as claimed in claim 2, in admixture or conjunction with a pharmaceutically suitable carrier.

54. A pharmaceutical preparation which comprises the compound claimed in any one of claims 3 to 35, in admixture or conjunction with a pharmaceutically suitable carrier.

55. A pharmaceutical preparation which comprises the compound claimed in any one of claims 36 to 38, in admixture or conjunction with a pharmaceutically suitable carrier.

56. A pharmaceutical preparation which comprises the compound claimed in any one of claims 39 to 44, in admixture or conjunction with a pharmaceutically suitable carrier.

57. A preparation as claimed in any one of claims 52 to 56, which is in the form of a sterile aqueous solution containing the active substance in an amount of 0.01 to 10 μ grams per ml.

58. A preparation as claimed in any one of claims 52 to 56, which is in form suitable for inhalation.

59. A preparation as claimed in claim 58, which is in the form of an aerosol or spray solution.

60. A preparation as claimed in any one of claims 52 to 56, which is in a form suitable for oral administration.

61. A preparation as claimed in claim 60, which is in the form of a tablet, dragée or capsule.

62. A preparation as claimed in any one of claims 52 to 56, which is in a form suitable for parenteral administration.

63. A preparation as claimed in claim 62, which is in the form of a sterile aqueous or oily solution suitable for injection.

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